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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/915,814	07/26/2001	Madeline M. Butler	ISPH-0587	6393
36324	7590	03/24/2004	EXAMINER	
MARSHALL, GERSTEIN & BORUN 6300 SEARS TOWER 233 SOUTH WACKER DRIVE CHICAGO, IL 60606-6357			ZARA, JANE J	
			ART UNIT	PAPER NUMBER
			1635	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

SPM

<b>Office Action Summary</b>	<b>Application No.</b> 09/915,814	<b>Applicant(s)</b> BUTLER ET AL.	
	<b>Examiner</b> Jane Zara	<b>Art Unit</b> 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 02 January 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,4-70 and 72-83 is/are pending in the application.  
     4a) Of the above claim(s) 16-70 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-15, 72-83 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

This Office action is in response to the communication filed 1-2-04.

Claims 1, 2, 4-70, 72-83 are pending in the instant application. Claims 16-70 have been withdrawn as being drawn to a non-elected invention.

### ***Election/Restrictions***

This application contains claims 16-70 drawn to an invention nonelected with traverse in Paper No. 10-3-02. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

### ***Response to Arguments and Amendments***

#### **Withdrawn Rejections**

Any rejections not repeated in this Office action are hereby withdrawn.

#### **Maintained Rejections**

Claim 15 is rejected under 35 U.S.C. 112, first paragraph, for lacking enablement over the scope claimed, for the reasons of record set forth in the Office action mailed 7-29-03.

No arguments were presented addressing the scope of enablement rejection of claim 15. The invention is enabled for inhibiting that target hlp of SEQ ID NO:3 in vitro comprising the administration of antisense specifically targeting hlp of SEQ ID NO: 3.

The examples provided in the instant application are not representative of inhibiting the target gene hlp of SEQ ID NO: 3 in an organism comprising the administration, by any means, of the antisense claimed.

Claims 1, 2, 4-8, 11-15, 72-81 are rejected under 35 U.S.C. 102(a) as being anticipated by Mitchell et al for the reasons of record set forth in the Office action mailed 7-29-03.

Applicant's arguments filed 1-2-04 have been fully considered but they are not persuasive. Applicants argue that the cited reference fails to teach each and every limitation of the claims and therefore cannot anticipate the subject matter of the pending claims. Mitchell teaches antisense oligonucleotides between 8-50 nucleobases that specifically target and inhibit the expression of SEQ ID NO: 3 in vitro. Absent evidence to the contrary, the antisense designed according to the teachings of Mitchell would inherently possess the same functional activity as Applicant's claimed antisense. Therefore the instant 102 rejection is maintained.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Holst et al for the reasons of record set forth in the Office action mailed 7-29-03.

Applicant's arguments filed 1-2-04 have been fully considered but they are not persuasive. Applicants argue that the cited reference fails to teach each and every limitation of the claims and therefore cannot anticipate the subject matter of the pending claims. Contrary to Applicants' assertions, Holst teaches antisense oligonucleotides

between 8-50 nucleobases that specifically target and inhibit the expression of SEQ ID NO: 3 in vitro. Absent evidence to the contrary, the antisense designed according to the teachings of Holst would inherently possess the same functional activity as Applicant's claimed antisense. Therefore the instant 102 rejection is maintained.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Langin et al for the reasons of record set forth in the Office action mailed 7-29-03.

Applicant's arguments filed 1-2-04 have been fully considered but they are not persuasive. Applicants argue that the cited reference fails to teach each and every limitation of the claims and therefore cannot anticipate the subject matter of the pending claims. Contrary to Applicants' assertions, Langin teaches antisense oligonucleotides between 8-50 nucleobases that specifically target and inhibit the expression of SEQ ID NO: 3 in vitro. Absent evidence to the contrary, the antisense designed according to the teachings of Langin would inherently possess the same functional activity as Applicant's claimed antisense. Therefore the instant 102 rejection is maintained.

Claims 1, 2, 4-15, 72-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mitchell et al, Holst et al and Langin et al, and further in view of Milner and Baracchini et al for the reasons of record set forth in the Office action mailed 7-29-03.

Applicant's arguments filed 1-2-04 have been fully considered but they are not persuasive. Applicants argue that the limitations of the claimed invention were not

taught by Mitchell, Holst or Langin, and that the secondary references of Milner and Baracchini do not make up for the primary references' deficiencies. Contrary to Applicants' assertions, Mitchell, Holst and Langin teach antisense oligonucleotides between 8-50 nucleobases that specifically target and inhibit the expression of SEQ ID NO: 3 in vitro. Absent evidence to the contrary, the antisense designed according to the teachings of Mitchell, Holst and Langin would inherently possess the same functional activity as Applicant's claimed antisense.

Applicants also argue that Milner discloses a method to test heteroduplex formation between antisense candidates and their intended target in a test tube, and that it would be unpredictable to go from a test tube to a cell to determine antisense ability to target and inhibit a target gene. Contrary to Applicants' assertions, it would require routine experimentation to test antisense oligonucleotides for their ability to target and inhibit expression of a known and previously characterized target nucleic acid in a target cell line in vitro. The method of Milner teaches designing antisense for targeting regions essentially blanketing a target gene of known sequence, then testing for inhibition of expression of that target gene. The ability to then employ these techniques for designing antisense and determining levels of target gene expression in a target cell in vitro would not require undue experimentation and would be quite routine.

Applicants argue that Baracchini targets a completely different gene in a different cell line than those of the instantly claimed invention and therefore is inappropriate for applying toward the instant 103 rejection. Contrary to Applicants' assertions, Baracchini

has been cited to teach the general applicability of modifications incorporated into antisense to enhance their stability, target binding and cellular uptake, and so is an appropriate reference with regard to general antisense modifications. The modifications disclosed by Baracchini (e.g. phosphorothioate internucleotide linkages, nucleobase and sugar modifications, chimeric antisense, colloidal dispersions of antisense oligonucleotides) are not limited to an antisense of a particular sequence, but can be incorporated into antisense targeting any gene sequence. Therefore, the references, taken together, provide the general knowledge and motivation that render the claimed invention obvious to one of ordinary skill in the art.

### ***Conclusion***


Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765**. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

  
**RAM R. SHUKLA, PH.D.**  
**PRIMARY EXAMINER**